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EXAMINER	
NGUYEN, QUANG	

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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,705	CHRIST ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,11,12,15,19-23,25-36,38 and 42-44* is/are pending in the application.

4a) Of the above claim(s) *12,15,23,31,32,34,38 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,11,19-22,25-30,33,35,36,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/06;8/30/07;4/21/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 7-9, 11-12, 15, 19-23, 25-36, 38 and 42-44 are pending in the present application.

Applicant's election without traverse of Group I in the reply filed on 4/21/2010 is acknowledged. Applicants further elected the following species: (a) penile smooth muscle; (b) maxi K as the elected potassium channel protein; (c) naked DNA transfer; and (d) erectile dysfunction.

Claims 12, 15, 23, 31-32, 34, 38, 42 are withdrawn from further consideration because they are directed to non-elected species.

Accordingly, claims 1, 7-9, 11, 19-22, 25-30, 33, 35-36 and 43-44 are examined on the merits herein **with the above elected species**.

Claim Objections

Claims 1 and 35 are objected to because of the phrase "a DNA sequence comprising a smooth muscle specific promoter, smooth muscle alpha actin (SMAA), operably linked to a sequence encoding a maxi-K". This is because the term "smooth muscle alpha actin" by itself is not necessarily referred to a smooth muscle alpha actin promoter. To overcome this objection, the examiner suggests the insertion of the term "promoter" immediately after the term "(SMAA)" in the above phrase.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims are rejected under 35 U.S.C. 112, first paragraph, because **with respect to the elected species** the specification, while being enabling for:

A method for **enhancing corporal smooth muscle relaxation** in a subject, comprising **introducing directly** a DNA sequence comprising a smooth muscle specific promoter operably linked to a sequence encoding a maxi-K potassium channel protein, into corporal smooth muscle cells of said subject to enhance corporal smooth muscle relaxation;

does not reasonably provide enablement for a method of regulating penile smooth muscle tone or treating erectile dysfunction in a subject as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The instant specification is not enabled for a method of regulating penile smooth muscle tone in a subject or a method of treating erectile dysfunction in a subject as broadly claimed for the reasons discussed below.

1. The breadth of the claims

With respect to the elected species, the claims are directed to a method of regulating penile smooth muscle tone or treating erectile dysfunction in a subject comprising introducing and expression of a DNA sequence comprising a smooth muscle specific promoter, including smooth muscle alpha actin (SMAA) promoter, operably linked to a sequence encoding a maxi-K potassium channel protein in a sufficient number of penile smooth muscle cells of the subject to regulate penile smooth muscle tone in the subject. It is noted that the term "regulation" as defined by the instant specification to be meant modulation (increase or decrease) relaxation or modulaton (increase or decrease) of contraction (paragraph 22). Therefore, **the instant claims encompass increased or decreased relaxation and/or increased or decreased contraction of corporal (penile) smooth muscles via an expressing a recombinant vector encoding a maxi-K potassium channel protein in a subject; and that the DNA sequence can be introduced into a subject at any site and/or by any route in a subject**.

2. The state of the prior art and the unpredictability of the prior art

At about the effective filing date of the present application (11/26/2003), the attainment of any therapeutic effect via gene therapy was and remains highly unpredictable. **There are several known factors that limit an effective human gene**

therapy, including sub-optimal vectors, the lack of a stable *in vivo* transgene expression, the adverse host immunological responses to the delivered vectors and most importantly an efficient gene delivery to target tissues or cells. Romano et al. (Stem Cells 18:19-39, 2000) state "The potential therapeutic applications of gene transfer technology are enormous. However, **the effectiveness of gene therapy programs is still questioned**", and "[d]espite the latest significant achievements reported in vector design, **it is not possible to predict to what extent gene therapeutic interventions will be effective in patients, and in what time frame**" (see abstract, col. 2). Verma et al. (Annu. Revi. Biochem. 74:711-738, 2005) state "The young field of gene therapy promises major medical progress toward the cure of a broad spectrum of human diseases, ranging from immunological disorders to heart disease and cancer. It has, therefore, generated great hopes and great hypes, but **it has yet to deliver its promised potential**", and "[I]f scientists from many different disciplines participate and pull together as a team to tackle the obstacles, **gene therapy will be added to our medicinal armada** and the ever-expanding arsenal of new therapeutic modalities." (page 732, top of third paragraph). Goncalves (BioEssays 27:506-517, 2005) also states "Overall, one can conclude that further improvements in gene transfer technologies (e.g. control over transgene expression and integration) and deeper insights in host-vector interactions (e.g. knowledge on vector and gene-modified cell bio-distribution following different routes of administration and the impact on innate and adaptive immunity) are warranted before clinical gene therapy reaches maturity" (page 514, right-hand column, last paragraph). Gardlik et al. (Med. Sci. Monit.

11:RA110-121, 2005) conclude "Although clinical trials have already started, **there are still numerous limitations that must be solved before routine clinical use**. Nevertheless, it can be expected that **future research will bring tissue- and disease-specific delivery strategies and that this hurdle will be overcome at last**" (page RA119, right-hand column, last paragraph).

Additionally, at the effective filing date of the present application both Geliebter et al (US 6,150,338; IDS) and Geliebter et al (US 7,030,096; IDS) have only demonstrated enhancing/increasing corporal (penile) smooth muscle relaxation in a subject via direct injection of a recombinant expression vector encoding a maxi-K potassium channel protein into penile smooth muscle cells of the subject.

3. The amount of direction or guidance provided

The instant specification fails to provide any guidance for a skilled artisan on how to overcome obstacles associated with *in vivo* vector targeting known in the gene therapy art, **so that at least a recombinant expression vector encoding a maxi-K potassium channel protein can be delivered at any site and/or by any route of delivery (e.g, oral, intravenous, topical, intramuscular or nebulization deliveries) in a treated subject and yet the recombinant expression vector can still reach to the targeted penile smooth muscle cells in an effective amount to yield the desired therapeutic effects**. There is also no evidence of record indicating that the heterologous expression of maxi-K potassium channel protein in the treated subject resulted in decreased corporal smooth muscle relaxation and/or increased corporal smooth muscle contraction, which are desired therapeutic results contemplated by

Applicants in the methods as broadly claimed. On the contrary, the instant specification teaches explicitly that a single intracorporal injection of DNA encoding hSlo resulted in an increased corporal smooth muscle relaxation (see at least paragraph 65 and Figure 2). Therefore, at least in light of the state of the gene therapy art and particularly the gene therapy art on treating penile or erectile dysfunction using a DNA encoding a potassium channel protein as discussed above, coupled with the lack of sufficient guidance provided by the instant specification it would have required undue experimentation for a skilled artisan to make and use the treatment method as broadly claimed.

Furthermore, the physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues set forth above, the state of the relevant gene therapy art, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7-9, 11, 19-22, 25-30, 33, 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, independent claims 1 and 35 recite the broad recitation “a smooth muscle specific promoter” and the claims also recite “smooth muscle alpha actin", which is the narrower statement of the range/limitation. When read in light of the instant specification and in the context of the instant claims, the term “smooth muscle alpha actin” refers to smooth muscle alpha actin promoter.

In claim 21, it is unclear what is encompassed by the phrase “wherein the DNA sequence is introduced using an EYFP vector”. This is because an EYFP vector

normally by itself does not contain a smooth muscle specific promoter and/or a sequence encoding a maxi-K. Please see the description of the pEYFP Vector Information from Clontech (Catalog #6004-1, 2002, pages 1-3). Then how can simply using an EYFP vector resulting in the introduction of a DNA sequence comprising a smooth muscle specific promoter operably linked to a sequence encoding a maxi-K? Clarification is requested because the metes and bounds of the claim as written are not clearly determined. For the purpose of a compact prosecution, the examiner interprets the claim to be that the DNA sequence is present in an EYFP vector.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 7-9, 11, 19-20, 22, 25-30, 30 and 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Geliebter et al (US 6,150,338; IDS).

Geliebter et al teach at least a method for enhancing corporal smooth muscle relaxation resulting in a more easily attained erection in a subject, including a subject having erectile dysfunction resulted from a variety of disorders including neurogenic,

arteriogenic and veno-occlusive dysfunctions, said method comprises directly injected into corporal smooth muscle cells of said subject with a DNA encoding a maxi-K potassium channel protein (hslo cDNA) in various forms, including a naked DNA expression plasmid vector, and wherein the expression plasmid vector can contain smooth muscle specific promoters and enhancers for expressing the encoded maxi-K potassium channel protein (see at least Summary of the Invention; particularly col. 4, lines 16-24, lines 53-65; col. 5, lines 24-44; col. 6, lines 9-49; examples and issued claims).

The teachings of Geliebter et al meet every limitation of the claims as broadly written. Therefore, the reference anticipates the instant claims.

Claims 1, 7-9, 11, 19-20, 22, 25-30, 30 and 35-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Geliebter et al (US 7,030,096; IDS).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Geliebter et al teach at least a method for enhancing relaxation of corporal (penile) smooth muscle resulting in a more easily attained erection in a subject, including a subject having erectile dysfunction resulted from a variety of disorders

including neurogenic, arteriogenic and veno-occlusive dysfunctions, said method comprises directly injected into corporal smooth muscle cells of said subject with a DNA encoding a maxi-K potassium channel protein (hslo cDNA) in various forms, including a naked DNA expression plasmid vector, and wherein the expression plasmid vector can contain smooth muscle specific promoters (e.g., the SM22alpha promoter) and enhancers for expressing the encoded maxi-K potassium channel protein (see at least Summary of the Invention; particularly col. 9, line 54 continues to line 11 of col. 10; col. 10, lines 26-37; col. 11, lines 32-45; col. 13, line 7 continues to line 60 of col. 15; examples and issued claims).

The teachings of Geliebter et al meet every limitation of the claims as broadly written. Therefore, the reference anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 43, 35 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geliebter et al (US 6,150,338; IDS) in view of Leiden et al (US 6,436,907).

With respect to the elected species and within the scope of enablement, Geliebter et al teach at least a method for enhancing corporal smooth muscle relaxation resulting in a more easily attained erection in a subject, including a subject having erectile dysfunction resulted from a variety of disorders including neurogenic, arteriogenic and veno-occlusive dysfunctions, said method comprises directly injected into corporal smooth muscle cells of said subject with a DNA encoding a maxi-K potassium channel protein (hslo cDNA) in various forms, including a naked DNA expression plasmid vector, and wherein the expression plasmid vector can contain smooth muscle specific promoters and enhancers for expressing the encoded maxi-K potassium channel protein (see at least Summary of the Invention; particularly col. 4, lines 16-24, lines 53-65; col. 5, lines 24-44; col. 6, lines 9-49; examples and issued claims).

Geliebter et al do not teach specifically the use of a smooth muscle alpha actin (SMAA) promoter for expressing the encoded maxi-K potassium channel protein, even though Geliebter et al teach explicitly using smooth muscle specific promoters and enhancers.

At the effective filing date of the present application (11/26/2003), Leiden et al already taught at **least the use of a smooth muscle alpha-actin promoter for expressing a desired gene product into vascular smooth muscle cells in both *in vitro* and *in vivo*** (see at least Brief Summary of the Invention; particularly col. 9, line 49 continues to line 11 of col. 10).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the method taught by Geliebter et al by also selecting a smooth muscle alpha-actin promoter for expressing hslo cDNA in corporal smooth muscle cells in light of the above teachings of Leiden et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because a smooth muscle alpha-actin promoter has been used to express a desired gene product in smooth muscle cells as taught by Leiden et al. Furthermore, please note that Geliebter et al already taught explicitly that any smooth muscle specific promoter can be used.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Geliebter et al., Leiden et al; coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geliebter et al (US 6,150,338; IDS) in view of pEYFP Vector Information from Clontech (Catalog #6004-1, 2002, pages 1-3).

With respect to the elected species and within the scope of enablement, Geliebter et al teach at least a method for enhancing corporal smooth muscle relaxation resulting in a more easily attained erection in a subject, including a subject having erectile dysfunction resulted from a variety of disorders including neurogenic, arteriogenic and veno-occulusive dysfunctions, said method comprises directly injected into corporal smooth muscle cells of said subject with a DNA encoding a maxi-K potassium channel protein (hslo cDNA) in various forms, including a naked DNA expression plasmid vector, and wherein the expression plasmid vector can contain smooth muscle specific promoters and enhancers for expressing the encoded maxi-K potassium channel protein (see at least Summary of the Invention; particularly col. 4, lines 16-24, lines 53-65; col. 5, lines 24-44; col. 6, lines 9-49; examples and issued claims). Geliebter et al further disclose that vectors suitable for the expression of hslo cDNA would be apparent to one skilled in the art and they include pET-3d, pcDNA, pcDNA3, pREP10, pRc/CMV among others (col. 5, line 59 continues to line 8 of col. 6).

Geliebter et al do not teach specifically that the expression cassette of hslo cDNA under the expression control of a smooth muscle specific promoter is in a pEYFP vector.

At the effective filing date of the present application (11/26/2003), pEYFP vector was already commercially available from Clontech and its description was available in the Catalog #6004-1.

Accordingly, it would also have been obvious for an ordinary skilled artisan to modify the method taught by Geliebter et al by also having an expression cassette of hslo cDNA under the expression control of a smooth muscle specific promoter to be in a pEYFP vector.

An ordinary skilled artisan would have been motivated to carry out the above modification because pEYFP vector was already commercially available from Clontech. Furthermore, please note that Geliebter et al already taught explicitly that any suitable vector for expression from a variety of sources can be used and that it would be apparent to one skilled in the art.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Geliebter et al., pEYFP Vector Information from Clontech; coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7-9, 11, 19-20, 22, 25-30, 33, 35-36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7,030,096.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of enhancing relaxation of a penile smooth muscle in a subject having heightened contractility of the penile smooth muscle, comprising the direct introduction and expression of a DNA sequence (in the form of a naked DNA) comprising a promoter sequence, including a smooth muscle specific promoter, operably linked to a sequence encoding maxi-K potassium channel protein into a sufficient number of penile smooth muscle cells of the subject in US 7,030,096 anticipate the claimed genus in the application being examined and, therefore, a patent to the genus would, necessarily, extend the rights of the species or sub- should the genus issue as a patent after the species of sub-genus.

Claims 1, 7-9, 11, 19-20, 22, 25-30, 30 and 35-36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,150,338. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons discussed below.

With respect to the elected species, the instant claims are directed to a method for regulating penile smooth muscle tone in a subject, comprising the introduction and expression of a DNA sequence comprising a smooth muscle specific promoter operably linked to a sequence encoding a maxi-K potassium channel protein that regulates penile smooth muscle tone in a sufficient number of penile smooth muscle cells of the subject.

Claims 1-9 of US 6,150,338 are drawn to a method for inducing penile erection in a subject comprising the introduction and expression of a DNA sequence encoding a

maxi-K potassium channel protein into a sufficient number of penile cells of the subject to induce penile erection in the subject.

The claims of the present application differ from the issued claims of US Patent No. 6,150,338 in reciting specifically a smooth muscle specific promoter operably linked to a sequence encoding a maxi-K.

The claims of the present application can not be considered to be patentably distinct over claims 1-9 of U.S. Patent No. 6,150,338 when there is a specific disclosed embodiment of the issued U.S. patent that teaches using smooth muscle specific promoters and enhancers for expression (col. 6, lines 34-35). Accordingly, the claims of U.S. Patent No. 6,150,338 fall within the scope of claims 1, 7-9, 11, 19-20, 22, 25-30, 30 and 35-36 of the present application.

This is because it would have been obvious to an ordinary skilled artisan to modify the claims of U.S. Patent No. 6,150,338 by also using smooth muscle specific promoters for expressing a DNA sequence encoding a maxi-K potassium channel protein into penile smooth muscle cells of a subject in need thereof, that support the instant claims. An ordinary skilled artisan would have been motivated to do this because this specific embodiment is explicitly disclosed or taught in of U.S. Patent No. 6,150,338 as a preferred embodiment.

Claims 43-44 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,150,338 in view of Leiden et al (US 6,436,907).

Claims 43-44 of the present application differ from the issued claims of US Patent No. 6,150,338 in reciting specifically using the smooth muscle specific promoter SMAA.

However, at the effective filing date of the present application (11/26/2003), Leiden et al already taught at **least the use of a smooth muscle alpha-actin promoter for expressing a desired gene product into vascular smooth muscle cells in both *in vitro* and *in vivo*** (see at least Brief Summary of the Invention; particularly col. 9, line 49 continues to line 11 of col. 10).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the method taught US 6,436,907 by also selecting a smooth muscle alpha-actin promoter for expressing hslo cDNA in corporal smooth muscle cells

An ordinary skilled artisan would have been motivated to carry out the above modification because a smooth muscle alpha-actin promoter has been used to express a desired gene product in smooth muscle cells as taught by Leiden et al. Furthermore, please note that US 6,436,907 already taught explicitly that any smooth muscle specific promoter can be used.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of US 6,436,907, Leiden et al; coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

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/Quang Nguyen/

Primary Examiner, AU 1633